

Amendments to the Specification:

Please add the following paragraph on page 1, line 2, immediately before the heading "FIELD OF THE INVENTION."

RELATED APPLICATIONS

This application is a continuation of U.S. Patent Application No. 09/032,972 filed on February 26, 1998. This application is incorporated herein by reference in its entirety.

Please replace the paragraph at page 7, line 35 to page 8, line 2 with the following.

In other preferred embodiments of the methods of the invention, the solvent in step (c) is a halogenated aromatic solvent or a halogenated alkyl aromatic solvent, with chlorobenzene or ~~benzotrifluoride~~ benzotrifluoride being especially preferred.

Please replace the paragraph at page 8, lines 7-10 with the following.

In further preferred embodiments of the method of the invention, the activated phosphorus compound is a 5'-protected ~~nucleoside~~ nucleoside phosphoramidite or a 5'-protected activated H-phosphonate nucleoside.

Please replace the paragraph at page 8, lines 11-19 with the following.

In some preferred embodiments of the methods of the invention, the 5'-protecting group of the 5'-O-protected nucleoside and the 5'-protected activated phosphorus compound is independently trityl, monomethoxy trityl, dimethoxytrityl, trimethoxytrityl, 2-chlorotrityl, DATE, TBTr, Pixyl or Moxyl, with trityl, monomethoxy trityl, dimethoxy trityl, 9-phenylxanthine-9-yl (Pixyl) or 9-(p-methoxyphenyl)xanthine-9-yl (MOX) being more preferred, and dimethoxy trityl being especially preferred.

Please replace the paragraph at page 9, line 37 to page 10 line 4 with the following.

In other preferred embodiments of the methods of the invention, the solvent in step (c) is a halogenated aromatic solvent or a halogenated alkyl aromatic solvent, with chlorobenzene or ~~benzotrifluoride~~ benzotrifluoride being especially preferred.

Please replace the paragraph at page 10, lines 9-12 with the following.

In further preferred embodiments of the method of the invention, the activated phosphorus compound is a 5'-protected ~~nucleoside~~ nucleoside phosphoramidite or a 5'-protected activated H-phosphonate nucleoside.

Please replace the paragraph at page 10, lines 14-21 with the following.

In some preferred embodiments of the methods of the invention, the 5'-protecting group of the 5'-O-protected nucleoside and the 5'-protected activated phosphorus compound is independently trityl, monomethoxy trityl, dimethoxytrityl, trimethoxytrityl, 2-chlorotrityl, DATE, TBTr, Pixyl or Moxyl, with trityl, monomethoxy trityl, dimethoxy trityl, 9-phenylxanthine-9-yl (Pixyl) or 9-(p-methoxyphenyl)xanthine-9-yl (MOX) being more preferred, and dimethoxy trityl being especially preferred.

Please replace the paragraph at page 16, lines 6-11 with the following.

Solid supports according to the invention include those generally known in the art to be suitable for use in solid phase methodologies, including, for example, controlled pore glass (CPG), oxalyl-controlled pore glass (see, e.g., Alul, et al., Nucleic Acids Research 1991, 19, 1527), TentaGel® ~~TentaGel~~ Support (an aminopolyethyleneglycol derivatized support (see, e.g., Wright, et al., Tetrahedron Letters 1993, 34, 3373)) and Poros® ~~Peros~~ (a copolymer of polystyrene/divinylbenzene).

Please replace the paragraph at page 16, lines 6-11 with the following.

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The term aromatic solvent is intended to denote aromatic compounds that are known to be useful as solvents in the art. These include for example, substituted and ~~unsubstituted~~ unsubstituted benzene, pyrrole, furan, and tetrahydrofuran, where the substituents include halogen, nitro, or hydroxymethyl.

Please replace the paragraph at page 21, lines 16-22 with the following.

In preferred embodiments of the invention, the 5'-protecting group is trityl, monomethoxy trityl, dimethoxytrityl, trimethoxytrityl, 2-chlorotrityl, DATE, TBTr, Pixyl or Moxyl, with trityl, monomethoxy trityl, dimethoxy trityl, 9-phenylxanthine-9-yl (Pixyl) or 9-(p-methoxyphenyl)xanthine-9-yl (MOX) being more preferred, and with dimethoxy trityl being especially preferred.

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1-41 (canceled)

42 (new). An improved process for solid phase oligonucleotide synthesis, the improvement comprising detritylating the nascent oligonucleotide having one or more trityl group in an arene solvent.

43 (new). The improved process according to claim 42, wherein the arene solvent is an alkylbenzene.

44 (new). The improved process according to claim 43, wherein the alkylbenzene has from about 1 to about 4 phenyl groups.

45 (new). The improved process according to claim 44, wherein the alkylbenzene has from about one to about three alkyl substituents.

46 (new). The improved process according to claim 45, wherein each alkyl group independently has from about 1 to about 6 carbon atoms.

47 (new). The improved process according to claim 46, wherein each alkyl group is a methyl group.

48 (new). The improved process according to claim 47, wherein the solvent is toluene, xylene, or combinations thereof.

49 (new). The improved process according to claim 42, wherein the detritylation is effected by a protic acid.

50 (new). The improved process according to claim 49, wherein the protic acid is DCA or TCA.

51 (new). The improved process of claim 50 wherein at least one trityl group is selected from trityl, monomethoxy trityl, dimethoxy trityl, 9-phenylxanthine-9-yl or 9-(p-methoxyphenyl)xanthine-9-yl.

52 (new). A method for preparing oligonucleotides comprising deprotecting a 5'-O-protected nucleoside that is attached to a solid support, wherein:

said protecting group is trityl, monomethoxy trityl, dimethoxytrityl, trimethoxytrityl, 2-chlorotrityl, 1,1-dianisyl-2,2,2-trichloroethyl (DATE), 4,4',4''-tris(benzoyloxyphenyl)methyl (TBTr), 9-phenylxanthine-9-yl (Pixyl) or 9-(p-methoxyphenyl)xanthine-9-yl (MOX); and

said deprotection is effected in an aromatic solvent, an alkyl aromatic solvent, a halogenated aromatic solvent, a halogenated alkyl aromatic solvent, or an aromatic ether solvent.

53 (new). The method of claim 52 wherein the protecting group is trityl, monomethoxy trityl, dimethoxy trityl, 9-phenylxanthine-9-yl (Pixyl) or 9-(p-methoxyphenyl)xanthine-9-yl.

54 (new). The method of claim 52 wherein said protecting group is trityl.

55 (new). The method of claim 52 wherein said protecting group is monomethoxy trityl.

56 (new). The method of claim 52 wherein said protecting group is dimethoxytrityl.

57 (new). The method of claim 52 wherein said protecting group is trimethoxytrityl.

58 (new). The method of claim 52 wherein said protecting group is 2-chlorotrityl.

59 (new). The method of claim 52 wherein said protecting group is 1,1-dianisyl-2,2,2-trichloroethyl (DATE).

60 (new). The method of claim 52 wherein said protecting group is 4,4',4"-tris(benzoyloxyphenyl)methyl (TBTr).

61 (new). The method of claim 52 wherein said protecting group is 9-phenylxanthine-9-yl (Pixyl).

62 (new). The method of claim 52 wherein said protecting group is 9-(p-methoxyphenyl)xanthine-9-yl (MOX).

63 (new). The method of claim 52 wherein the solvent is benzene, toluene, benzonitrile, o-xylene, m-xylene, p-xylene, mesitylene, or diphenyl ether.

64 (new). The method of claim 52 wherein said deprotection is effected in an aromatic solvent.

65 (new). The method of claim 52 wherein said deprotection is effected in an alkyl aromatic solvent.

66 (new). The method of claim 52 wherein said deprotection is effected in a halogenated aromatic solvent.

67 (new). The method of claim 52 wherein said deprotection is effected in a halogenated alkyl aromatic solvent.

68 (new). The method of claim 52 wherein said deprotection is effected in an aromatic ether solvent.

69 (new). The method of claim 52 wherein said deprotection is effected in o-xylene, m-xylene, p-xylene, mesitylene, or diphenyl ether.

70 (new). The method of claim 52 wherein said deprotection is effected in benzene, toluene, o-xylene, m-xylene, or p-xylene.

71 (new). The method of claim 52 wherein said deprotection is effected in toluene.

72 (new). The method of claim 52 wherein said deprotection is effected in a halogenated aromatic solvent or a halogenated alkyl aromatic solvent.

73 (new). The method of claim 52 wherein said deprotection is effected in chlorobenzene or benzonitrile.

74 (new). The method of claim 52 wherein said deprotection occurs in the presence of a protic acid.

75 (new). The method of claim 74 wherein the protic acid is formic acid, acetic acid, chloroacetic acid, dichloroacetic acid, trichloroacetic acid, trifluoroacetic acid, benzenesulfonic acid, toluenesulfonic acid, or phenylphosphoric acid.

76 (new). The method of claim 74 wherein the protic acid is dichloroacetic acid or trichloroacetic acid.

77 (new). A method of deprotecting a 5'-O-protected nucleoside in an oligonucleotide, wherein:

said nucleoside bears a trityl, monomethoxy trityl, dimethoxytrityl, trimethoxytrityl, 2-chlorotrityl, 1,1-dianisyl-2,2,2-trichloroethyl (DATE), 4,4',4''-tris(benzoyloxyphenyl)methyl (TBTr), 9-phenylxanthine-9-yl (Pixyl) or 9-(p-methoxyphenyl)xanthine-9-yl (MOX) protecting group; and

said deprotection is effected in the presence of an aromatic solvent, an alkyl aromatic solvent, a halogenated aromatic solvent, a halogenated alkyl aromatic solvent, or an aromatic ether solvent.

78 (new). The method of claim 77 wherein the protecting group is trityl, monomethoxy trityl, dimethoxy trityl, 9-phenylxanthine-9-yl (Pixyl) or 9-(p-methoxyphenyl)xanthine-9-yl.

79 (new). The method of claim 77 wherein said protecting group is trityl.

80 (new). The method of claim 77 wherein said protecting group is monomethoxy trityl.

81 (new). The method of claim 77 wherein said protecting group is dimethoxytrityl.

82 (new). The method of claim 77 wherein said protecting group is trimethoxytrityl.

83 (new). The method of claim 77 wherein said protecting group is 2-chlorotrityl.

84 (new). The method of claim 77 wherein said protecting group is 1,1-dianisyl-2,2,2-trichloroethyl (DATE).

85 (new). The method of claim 77 wherein said protecting group is 4,4',4''-tris(benzoyloxyphenyl)methyl (TBTr).

86 (new). The method of claim 77 wherein said protecting group is 9-phenylxanthine-9-yl (Pixyl).

87 (new). The method of claim 77 wherein said protecting group is 9-(p-methoxyphenyl)xanthine-9-yl (MOX).

88 (new). The method of claim 77 wherein the solvent is benzene, toluene, benzonitrile, o-xylene, m-xylene, p-xylene, mesitylene, or diphenyl ether.

89 (new). The method of claim 77 wherein said deprotection is effected in an aromatic solvent.

90 (new). The method of claim 77 wherein said deprotection is effected in an alkyl aromatic solvent.

91 (new). The method of claim 77 wherein said deprotection is effected in a halogenated aromatic solvent.

92 (new). The method of claim 77 wherein said deprotection is effected in a halogenated alkyl aromatic solvent.

93 (new). The method of claim 77 wherein said deprotection is effected in an aromatic ether solvent.

94 (new). The method of claim 77 wherein said deprotection is effected in o-xylene, m-xylene, p-xylene, mesitylene, or diphenyl ether.

95 (new). The method of claim 77 wherein said deprotection is effected in benzene, toluene, o-xylene, m-xylene, or p-xylene.

96 (new). The method of claim 77 wherein said deprotection is effected in toluene.

97 (new). The method of claim 77 wherein said deprotection is effected in a halogenated aromatic solvent or a halogenated alkyl aromatic solvent.

98 (new). The method of claim 77 wherein said deprotection is effected in chlorobenzene or benzonitrile.

99 (new). The method of claim 77 wherein the deprotection occurs in the presence of a protic acid.

100 (new). The method of claim 99 wherein the protic acid is formic acid, acetic acid, chloroacetic acid, dichloroacetic acid, trichloroacetic acid, trifluoroacetic acid, benzenesulfonic acid, toluenesulfonic acid, or phenylphosphoric acid.

101 (new). The method of claim 99 wherein the protic acid is dichloroacetic acid or trichloroacetic acid.

102 (new). The method of claim 77 wherein said nucleoside is bound to a solid support.

103 (new). A method comprising deprotecting a 5'-hydroxyl of a nucleoside wherein:

said nucleoside bears a trityl, monomethoxy trityl, dimethoxytrityl, trimethoxytrityl, 2-chlorotrityl, 1,1-dianisyl-2,2,2-trichloroethyl (DATE), 4,4',4''-tris(benzoyloxyphenyl)methyl (TBTr), 9-phenylxanthine-9-yl (Pixyl) or 9-(p-methoxyphenyl)xanthine-9-yl (MOX) protecting group; and

said deprotection is effected in the presence of an aromatic solvent, an alkyl aromatic solvent, a halogenated aromatic solvent, a halogenated alkyl aromatic solvent, or an aromatic ether solvent.

104 (new). The method of claim 103 wherein the protecting group is trityl, monomethoxy trityl, dimethoxy trityl, 9-phenylxanthine-9-yl (Pixyl) or 9-(p-methoxyphenyl)xanthine-9-yl.

105 (new). The method of claim 103 wherein said protecting group is trityl.

106 (new). The method of claim 103 wherein said protecting group is monomethoxy trityl.

107 (new). The method of claim 103 wherein said protecting group is dimethoxytrityl.

108 (new). The method of claim 103 wherein said protecting group is trimethoxytrityl.

109 (new). The method of claim 103 wherein said protecting group is 2-chlorotrityl.

110 (new). The method of claim 103 wherein said protecting group is 1,1-dianisyl-2,2,2-trichloroethyl (DATE).

111 (new). The method of claim 103 wherein said protecting group is 4,4',4''-tris(benzoyloxyphenyl)methyl (TBTr).

112 (new). The method of claim 103 wherein said protecting group is 9-phenylxanthine-9-yl (Pixyl).

113 (new). The method of claim 103 wherein said protecting group is 9-(p-methoxyphenyl)xanthine-9-yl (MOX).

114 (new). The method of claim 103 wherein the solvent is benzene, toluene, benzonitrile, o-xylene, m-xylene, p-xylene, mesitylene, or diphenyl ether.

115 (new). The method of claim 103 wherein said deprotection is effected in an aromatic solvent.

116 (new). The method of claim 103 wherein said deprotection is effected in an alkyl aromatic solvent.

117 (new) The method of claim 103 wherein said deprotection is effected in a halogenated aromatic solvent.

118 (new). The method of claim 103 wherein said deprotection is effected in a halogenated alkyl aromatic solvent.

119 (new). The method of claim 103 wherein said deprotection is effected in an aromatic ether solvent.

120 (new). The method of claim 103 wherein said deprotection is effected in o-xylene, m-xylene, p-xylene, mesitylene, or diphenyl ether.

121 (new). The method of claim 103 wherein said deprotection is effected in benzene, toluene, o-xylene, m-xylene, or p-xylene.

122 (new). The method of claim 103 wherein said deprotection is effected in toluene.

123 (new). The method of claim 103 wherein said deprotection is effected in a halogenated aromatic solvent or a halogenated alkyl aromatic solvent.

124 (new). The method of claim 103 wherein said deprotection is effected in chlorobenzene or benzonitrile.

125 (new). The method of claim 103 wherein the deprotection occurs in the presence of a protic acid.

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126 (new). The method of claim 125 wherein the protic acid is formic acid, acetic acid, chloroacetic acid, dichloroacetic acid, trichloroacetic acid, trifluoroacetic acid, benzenesulfonic acid, toluenesulfonic acid, or phenylphosphoric acid.

127 (new). The method of claim 125 wherein the protic acid is dichloroacetic acid or trichloroacetic acid.

128 (new). The method of claim 103 wherein said nucleoside is bound to a solid support.